

A2 Depending on the assay, a Fluorometric Imaging Plate Reader (FLIPR™) instrument (Molecular Devices, Sunnyvale, CA) is often the instrument of choice for fluorescence-based assays of the invention. The FLIPR™ system (Molecular Devices, Sunnyvale, CA) has the following desirable features: (i) It uses a combination of a water-cooled, argon-ion laser illumination and cooled CCD camera as an integrating detector that accumulates detectable signal over the period of time in which it is exposed to the image and, as a result, its signal-to-noise characteristics are generally superior to those of conventional imaging optics; (ii) it also makes use of a proprietary cell-layer isolation optics that allow signal discrimination on a cell monolayer, thus reducing undesirable extracellular background fluorescence; (iii) it provides data in real-time, and can also provide kinetic data (*i.e.*, readings at a plurality of timepoints); (iv) it has the ability to simultaneously excite fluorophores in, and read emissions from, all 96 wells of a 96-well microplate; (v) it provides for precise control of temperature and humidity of samples during analysis; (vi) it includes an integrated state-of-the-art 96-well pipettor, which uses dispensable tips to eliminate carryover between experiments, and that can be used to aspirate, dispense and mix precise volumes of fluids from microplates; and, (vii) in the case of the FLIPR<sup>384</sup> instrument, it can be adapted to run sample assays in a robotic or semi-robotic fashion, thus providing for rapid HTS analysis of large numbers of samples (*e.g.*, up to about a hundred 96-well microplates per day).

Please amend the paragraph at page 70, line 20 through page 71, line 21 to read as follows:

A2 A variety of apoptogens are known to those familiar with the art and may include by way of illustration herbimycin A (Mancini et al., *J. Cell. Biol.* 138:449-469, 1997); paraquat (Costantini et al., *Toxicology* 99:1-2, 1995); ethylene glycols ([www.ulaval.ca/vrr/rech/Proj/532866.html](http://www.ulaval.ca/vrr/rech/Proj/532866.html)); protein kinase inhibitors such as, *e.g.*: staurosporine, calphostin C, caffeic acid phenethyl ester, chelerythrine chloride, 1-(5-isoquinolinesulfonyl)-2-methylpiperazine, N-[2-((*p*-bromocinnamyl)amino)ethyl]-5-5-isoquinolinesulfonamide, KN-93, genistein, quercetin and *d-erythro*-sphingosine derivatives; ultraviolet radiation; ionophores such as, *e.g.*, ionomycin, valinomycin and other ionophores known in the art; MAP kinase inducers such as, *e.g.*, anisomycin and anandamine; cell cycle blockers such as, *e.g.* aphidicolin, colcemid,

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5-fluorouracil and homoharringtonine; acetylcholinesterase inhibitors such as, *e.g.*, berberine; anti-estrogens such as, *e.g.*, tamoxifen; pro-oxidants such as, *e.g.*, tert-butyl peroxide and hydrogen peroxide; free radicals such as, *e.g.*, nitrous oxide; inorganic metal ions, such as, *e.g.*, cadmium; DNA synthesis inhibitors such as, *e.g.*, actinomycin D, bleomycin sulfate, hydroxyurea, methotrexate, mitomycin C, camptothecin, daunorubicin and DNA intercalators such as, *e.g.*, doxorubicin; protein synthesis inhibitors such as, *e.g.*, cycloheximide, puromycin, and rapamycin; agents that effect microtubule formation or stability such as, *e.g.*: vinblastine, vincristine, colchicine, 4-hydroxyphenylretinamide and paclitaxel; gangliosides such as GD3 (Scorrano et al., *J. Biol. Chem.* 274:22581-22585, 1999); agents that may be contacted with cells having appropriate receptors including, by way of example and not limitation, tumor necrosis factor (TNF), FasL, glutamate, NMDA (the preceding are contacted with cells having receptors that mediate the uptake of the indicated agent), corticosterone [with cells having mineral corticoid or glucocorticoid receptor(s)]; agents that are withdrawn from the culture media of cells after some period of time such as, by way of non-limiting example, the withdrawal of IL-2 from lymphocytes; and agents that can be contacted with isolated mitochondria or permeabilized cells including, by way of example and not limitation, calcium and inorganic phosphate, (Kroemer et al., *Ann. Rev. Physiol.* 60:619-642, 1998) and members of the Bax/Bcl-2 family of proteins (Jurgenmeier et al., *Proc. Natl. Acad. Sci. U.S.A.* 95:4997-5002, 1998). Such agents are prepared according to methods known in the art or are commercially available from companies such as, for example, Calbiochem (San Diego, CA) and Sigma Chemical Company (St. Louis, MO).

Please amend the paragraph at page 73, lines 9-27 to read as follows:

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Depending on the assay, a Fluorometric Imaging Plate Reader (FLIPR™) instrument (Molecular Devices, Sunnyvale, CA) is often the instrument of choice for the assays of the invention. The FLIPR™ (Molecular Devices, Sunnyvale, CA) has the following desirable features (see [www.moleculardevices.com/pages/flipr.html](http://www.moleculardevices.com/pages/flipr.html)): it uses a combination of a water-cooled, argon-ion laser illumination and cooled CCD camera as an integrating detector that accumulates signal over the period of time in which it is exposed to the image and, as a result, its signal-to-noise characteristics are generally superior to those of conventional imaging optics; it also makes use of a proprietary cell-layer isolation optics that allow signal discrimination on a